

AMENDMENTS TO THE CLAIMS

Listing of Claims:

(Cancelled) Claims 1 – 79

80. (Previously Presented) A bidentate motif capable of binding a cytoplasmic protein and activating cellular activities in a cell, said bidentate motif comprising a tyrosine and a serine/threonine residue which are capable of interaction with cytoplasmic proteins, and wherein the residue and cytoplasmic protein can interact to activate cellular activity in the cell.

81. (Previously Presented) A bidentate motif according to claim 80 wherein the tyrosine and serine/threonine residue comprises a binary switch for independent regulation of cellular activity.

82. (Currently Amended) A bidentate motif capable of binding to a cytoplasmic protein according to claim 80 comprising a tyrosine and a serine/threonine residue, said motif comprising an amino acid sequence alignment selected from the group consisting of:

N-X-X-Y-(X) 1-13-[R/K/H/Q]-[X/ψ] 2-3-S/T-X-P (SEQ ID NO: 71)

wherein X is any residue, Y is tyrosine, S/T is serine or threonine and ψ is a hydrophobic residue or an equivalent thereof; or

Y-(X) 1-16-[R/K/H/Q]-[X/ψ]2-3-S/T-X-P (SEQ ID NO: 72)

wherein X is any residue, Y is tyrosine, S/T is serine or threonine and ψ is a hydrophobic residue or an equivalent thereof; or

N-X-X-Y-[X]1-30-[R/K/Q'H]-[X]1-4-[S/T]-X-p (SEQ ID NO: 73)

wherein X is any residue, Y is phosphotyrosine, S/T is phosphoserine/phosphothreonine/phosphothreonine.

83. (Previously Presented) A bidentate motif according to claim 80 wherein the motif is derived from a receptor.

84. (Previously Presented) A bidentate motif according to claim 80 wherein the motif is derived from the common beta chain (β c).

85. (Previously Presented) A bidentate motif according to claim 80 wherein the tyrosine is equivalent to Tyr577 of the common beta chain (β c) and/or the serine is equivalent to Ser 585 of the common beta chain (β c).

86. (Previously Presented) A bidentate motif according to claim 80 wherein the tyrosine or serine/threonine are independently phosphorylated in response to a cytokine, and phosphorylation is dependent on the cytokine concentration.

87. (Previously Presented) A bidentate motif according to claim 80 wherein phosphorylation of the serine independently of the tyrosine regulates cell survival.

88. (Previously Presented) A bidentate motif according to claim 80 wherein phosphorylation of the tyrosine independent of the serine regulates cell survival and proliferation.

89. (Previously Presented) A bidentate motif according to claim 83, with a modification at a residue equivalent to the Tyr 577 and/or Ser585.

90. (Previously Presented) The bidentate motif according to claim 89 wherein the residue equivalent to Tyr 577 is substituted with phenylalanine and/or the Ser 585 residue is substituted with glycine.

91. (Currently Amended) A method of modulating cellular activity in a cell, said method comprising: modulating phosphorylation of a tyrosine and/or serine residue of a bidentate motif capable of binding to a cytoplasmic protein comprising a tyrosine and a serinelthreonine residue, said motif comprising an amino acid sequence alignment selected from the group consisting of:

N-X-X-Y-(X)₁₋₁₃-[R/K/H/Q]-[X/\psi]₂₋₃S/T-X-P
N-X-X-Y-(X)₁₋₁₃-[R/K/H/Q]-[X/\psi]₂₋₃S/T-X-P (SEQ ID NO: 71)

wherein X is any residue, Y is tyrosine, S/T is serine or threonine and \psi is a hydrophobic residue or an equivalent thereof; or

Y-(X)₁₋₁₆-[R/K/H/Q]-[X/\psi]₂₋₃S/T-X-P (SEQ ID NO: 72)

wherein X is any residue, Y is tyrosine, S/T is serine or threonine and \psi is a hydrophobic residue or an equivalent thereof; or

N-X-X-Y-[X]₁₋₃₀-[R/K/Q/H]-[X]₁₋₄[S/T]-X-p (SEQ ID NO: 73)

wherein X is any residue, Y is phosphotyrosine, S/T is phosphoserine/phosphothreonine.

92. (Previously Presented) A method according to claim 91 wherein the phosphorylation is modulated by mutating the tyrosine and/or serine.

93. (Currently Amended) A method according to claim 92 wherein the Tyrosine is substituted for phenylalanine and/or the serine is substituted for glycine.

94. (Previously Presented) A method according to claim 91 wherein the phosphorylation is decreased by subjecting the cell to an antagonist or kinase inhibitor which inhibits phosphorylation of the tyrosine and/or serine.

95. (Currently Amended) A method according to claim 91 wherein cellular activity is inhibited, said method comprising decreasing or inhibiting phosphorylation of the tyrosine and/or serine of the bidentate motif.

96. (Previously Presented) A method according to claim 95 wherein the cellular activity is cell survival, said method comprising inhibiting phosphorylation of the serine.

97. (Previously Presented) A method according to claim 95 wherein the cellular activity is cell survival, said method comprising inhibiting phosphorylation of the serine equivalent to Ser585 of the common β c.

98. (Previously Presented) A method according to claim 91 wherein cellular activity is activated, said method comprising inducing phosphorylation of the tyrosine and/or serine of the bidentate motif.

99. (Previously Presented) A method according to claim 98 wherein the cellular activity is cell survival, said method comprising increasing phosphorylation of the serine.

100. (Previously Presented) A method according to claim 91 wherein the cellular activity is cell proliferation, said method comprising increasing phosphorylation of the tyrosine.

101. (Currently Amended) A method of treating a cytokine mediated condition, said method comprising:

regulating activation of phosphorylation of a tyrosine and/or serine of a bidentate motif capable of binding to a cytoplasmic protein comprising a tyrosine and a serine/threonine residue, said motif comprising an amino acid sequence alignment selected from the group consisting of:

N-X-X-Y-(X)₁₋₁₃-(R/K/H/Q)-[X/\psi]₂₋₃-S/T-X-P (SEQ ID NO: 71)

wherein X is any residue, Y is tyrosine, S/T is serine or threonine and T/\psi is a hydrophobic residue or an equivalent thereof; or

Y-(X)₁₋₁₆-(R/K/H/Q)-(X/ψ)₂₋₃-(S/T)-X-P (SEQ ID NO: 72)

wherein X is any residue, Y is tyrosine, S/T is serine or threonine and ψ is a hydrophobic residue or an equivalent thereof; or

N-X-X-Y-(X)₁₋₃₀-(R/K/Q/H)-(X)₁₋₄-(S/T)-X-p (SEQ ID NO: 73)

wherein X is any residue, Y is phosphotyrosine, S/T is phosphoserine/phosphothreonine.

102. (Previously Presented) A method according to claim 101 wherein the cytokine mediated condition is treated by increasing or decreasing activation of phosphorylation of the tyrosine and/or serine of the bidentate motif.

103. (Previously Presented) A method according to claim 101 wherein the phosphorylation is decreased by mutating the tyrosine and/or serine.

104. (Previously Presented) A method use according to claim 103 wherein the motif is mutated by substituting tyrosine for phenylalanine and/or substituting serine for glycine.

105. (Previously Presented) A method according to claim 101 wherein the phosphorylation is decreased by subjecting the cell to an antagonist which inhibits phosphorylation of the tyrosine and/or serine.

106. (Previously Presented) A method according to claim 101 wherein the cytokine mediated condition is a GM-CSF mediated condition.

107. (Previously Presented) A method according to claim 101 wherein the cytokine mediated condition involves cell survival.

108. (Previously Presented) A method according to claim 101 wherein the cytokine mediated condition involves cell proliferation.

109. (Previously Presented) A method according to claim 101 wherein the cytokine mediated condition is selected from the group consisting of myeloid cell activation, asthma and rheumatoid arthritis.

110. (Currently Amended) A method for diagnosing a proliferative condition involving cell proliferation or cell survival, said method including:

detecting a level of phosphorylation of tyrosine and/or serine in a bidentate motif capable of binding to a cytoplasmic protein comprising a tyrosine and a serine/threonine residue, said motif comprising an amino acid sequence alignment selected from the group consisting of:

N-X-X-Y-(X)₁₋₁₃-[R/K/H/Q]-[X/ψ]₂₋₃-S/T-X-P (SEQ ID NO: 71)

wherein X is any residue, Y is tyrosine, S/T is serine or threonine and ψ is a hydrophobic residue or an equivalent thereof; or

Y-(X)₁₋₁₆-[R/K/H/Q]-[X/ψ]₂₋₃-S/T-X-P (SEQ ID NO: 72)

wherein X is any residue, Y is tyrosine, S/T is serine or threonine and ψ is a hydrophobic residue or an equivalent thereof; or

N-X-X-Y-[X]₁₋₃₀-[R/K/Q/H]-[X]₁₋₄-[S/T]-X-p (SEQ ID NO: 73)

wherein X is any residue, Y is phosphotyrosine, S/T is phosphoserine/phosphothreonine; and comparing against a cell of a normal level of phosphorylation.